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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KALLIS, RUSSELL	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/674,768	NEUHAUS ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-13-16-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-13-16-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/07/2003 has been entered.

Claims 1-19 are pending. Claims 2-3 and 14-15 were cancelled in paper #21 submitted 4/22/2003 and have been mistakenly listed as withdrawn in the amendment filed 11/07/2003. Claims 1, 4-13 and 16-19 are examined. Applicant is required to file a corrected amendment to the claims in the next response.

Specification

The attempt to incorporate subject matter into this application by reference to GenBank Accession Number (page 4, specification) is improper because GenBank Accession numbers can be updated at any time. Further, the sequence described (page 4, specification) by Kampfenkel *et al.* in FEBS Letters 374, 1995; pages 351-355; also submitted as GenBank Accession No. Z49227 has changed since publication. See also MPEP 2422.03 paragraph 8 beginning with 37 CFR 1.821(d).

Claim Objections

Claim 11 is objected to because of the following informalities: The term "amylase" in line 7 should be --amylose--. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-13 and 16-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims genetically modified plant cells comprising a foreign nucleic acid molecule encoding a plastidial ADP/ATP translocator integrated into the nuclear genome, transformed plants thereof and methods of producing increased starch and oil in transformed plants therewith.

Applicant describes PCR primers of SEQ ID NO: 1 and 2 for isolation of a cDNA encoding the AATP2 ADP/ATP translocator from *Arabidopsis* (Accession No. X94626); and incorporates through reference AATP1-cDNA from *Arabidopsis* (Example 2, Kampfenkel *et al.* also Accession No. Z49227); and AATP1 from *S. tuberosum* (Example 3 Accession No. Y10821).

Applicant does not describe any other foreign nucleic acid molecule encoding a plastidial ADP/ATP translocator.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a

genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicants fail to describe a representative number of foreign nucleic acid molecule encoding a plastidial ADP/ATP translocator falling within the scope of the claimed genus. Applicants only provide GenBank Accession numbers for two sequences from *Arabidopsis* and a GenBank accession number for one sequence from potato encoding plastidial ADP/ATP translocators that have all changed since their submission. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of foreign nucleic acid molecules encoding a plastidial ADP/ATP translocator. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for plastidial ADP/ATP translocator, it remains unclear what features identify a foreign nucleic acid molecule encoding a plastidial ADP/ATP translocator. Since the genus of foreign nucleic acid molecules encoding a plastidial ADP/ATP translocator has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Applicant asserts that the issue of adequately described sequence information is not key to the present application where Applicant's have found a use for a previously known category of genes and that they are entitled to broad coverage without being limited to some generic structural definition (response pages 1-2). Applicant is required to provide a written description of the invention. The invention claims plant cells and plants and methods that require the use of

nucleic acids. The broad coverage that applicant seeks is contingent upon the clarity provided in the specification with respect to a description of those materials essential for practicing the invention. As articulated above that is not evident.

Applicant asserts that the specification clearly states that any nucleic acid molecule encoding an ADP/ATP translocator can be used to achieve the results of the present invention (response page 2). Clearly the necessary structural features and necessary elements for plastidial ADP/ATP translocator activity have not been described in the specification.

Applicant asserts that the Examiner has acknowledged that the specification describes two cDNAs from *Arabidopsis* which encode ADP/ATP translocator proteins (response page 2) and argued that it was unclear if the potato and bacterial ADP/ATP translocator sequences were protein or DNA (response page 2). Applicant is directed to objections and arguments supra.

Applicant asserts that the Examiner's objections to the lack of a sequence listing and the incorporation through reference are misplaced because the specification sets forth a common functional feature that must be shared by the claimed genus of foreign nucleic acid molecules, namely a transport protein the catalyzes the transport of ATP into plastids and ADP out of plastids (response pages 2-3). This 'functional feature' does not describe what the invention is but rather indicates what the invention does. Further, Applicant's remarks to the reference to sequences by GenBank Accession number are addressed in the objection discussed supra (response page 3). Furthermore, Applicant has not addressed the Examiner's remarks concerning the lack of defining motifs or conserved regions that would define the broadly claimed genus.

Claims 1, 4-13 and 16-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for transgenic potato plants comprising the AATP1-cDNA from *Arabidopsis* showing increased levels of starch and percent amylose does not reasonably provide enablement for any plant cells or plants comprising any foreign nucleic acid molecule encoding any plastidial ADP/ATP translocator having any combination of increased levels of oil, starch and amylose or any methods of increasing yield in a transgenic plant or for the production of increased oil in a transformed plant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Applicant broadly claims genetically modified plant cells comprising a foreign nucleic acid molecule encoding a plastidial ADP/ATP translocator integrated into the nuclear genome, transformed plants thereof and methods of producing increased starch and oil and amylose content in transformed plants therewith.

Applicant teaches increases in plastidial ADP/ATP translocator mRNA in potato transformed with sense AATP1-cDNA from *Arabidopsis* (Example 2 page 29); decreases in plastidial ADP/ATP translocator mRNA in potato transformed with antisense AATP1-cDNA from *Arabidopsis* (Example 3 page 30); antisense-AATP1 transformed potato lines having less starch and lower percent amylose content than wild type potato and potato lines transformed with sense AATP1 showing increased levels of starch and higher percent amylose than wild type potato (Example 4, pages 30-31).

Applicant does not teach any increases in oil or both starch and oil and amylose content, in any plant transformed with a foreign nucleic acid molecule encoding a plastidial ADP/ATP translocator or methods thererof, or any method of increasing yield in a transgenic plant other than increased starch and percent amylose content in potato.

Engineering increases in oil in any plant or plant seed by any transgenic methods is highly unpredictable because there are multiple steps that may be require an increase in activity before any accommodation of increased flux through rate limiting steps would yield a discernable phenotype. Increases through an entire pathway that would sustain an increase in partitioning of reserves of either starch or oil are unknown and might require upregulating the entire pathway to overcome unknown regulatory factors. (Ohlrogge J. *et al.* Biochemical Society Transactions, 2000; Vol. 28, part 6, pages 567-573; from page 570, column 2 to column 1, page 571). See *In re Fisher,* 166 USPQ 18, 24(CCPA 1970) which teaches "That paragraph (35 USC 112, first) requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment

provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved."

Further, engineering increases in starch and oil levels in a plant is unpredictable because there are unknown quantitative metabolic interactions directly related to acquiring the desired phenotype. Increases in starch metabolism resulted in decreases in fatty acid metabolism in isolated amyloplasts of cauliflower buds suggesting that engineering increases in both oil and starch content in a plant is not possible (Mohlmann T. *et al.* Planta, 1994 Vol. 194; pages 492-497; see page 496 column 1st full paragraph and column 2, 2nd full paragraph).

In addition, the isolation of any DNA sequences encoding a plastidial ADP/ATP translocator from any species introduces an element of unpredictability. The limitation is introduced in finding homologous regions that would adequately enable either PCR amplification or southern hybridization and would entail using either degenerate primers or probes with limited sequence identity. Thus the screen for DNA sequences encoding nonsymbiotic plant hemoglobin from any species sequences would isolate many genes other than those of interest. The inherent unpredictability in isolation of a homologous DNA sequence encoding a plastidial ADP/ATP translocator from any species is illustrated in an example where a small number of changes to the coding region for a strict desaturase resulted in an enzyme with a hydroxylase activity and that a small number of changes to the coding region of a desaturase could account for functional divergence seen across a range of enzymes involved in fatty acid

metabolism that have different specific activities (Broun P. *et al.* Science, Vol. 282; 13 November 1998, pp. 1315-1317; Abstract lines 4-6 and p. 1317 column 1, lines 37-56).

Based upon Applicant's limited guidance in the instant specification undue trial and error experimentation would be required by one of skill in the art to isolate and screen a multitude of non-exemplified DNA sequences encoding a plastidial ADP/ATP translocator and test for increases in oil and starch and amylose content by transformation of a myriad of non-exemplified plant species and to screen a multitude of transformed plants to select for the claimed phenotype based upon non-exemplified oil levels. Further, the specification is not enabling for the use of any foreign nucleic acid molecule encoding a plastidial ADP/ATP translocator because Applicant has not taught how to use any foreign nucleic acid molecule encoding a plastidial ADP/ATP translocator in a whole plant to achieve an increased oil content.

Given the unpredictability in isolating DNA sequences encoding foreign nucleic acid molecule encoding a plastidial ADP/ATP translocator from any species or in determining which pathways in which plants or plant tissues would allow for increased levels of starch and oil or increased starch, oil and amylose content when expressing a non-exemplified foreign nucleic acid molecule encoding a plastidial ADP/ATP translocator; the breadth of claims encompassing any levels of increased starch and oil and amylose content or any combination thereof in any plant in any plant tissue during any time in plant development; the lack of guidance in the examples of the specification or the prior art; and the undue trial and error experimentation required to practice the claimed invention, the invention is not enabled for the full scope of the claims.

The rejection of Claims 1, 4-13 and 16-19 under 35 U.S.C. 112 1st paragraph, enablement, with respect to the arguments presented in reference to Willmitzer and Anderson, and with respect to the polyploidal and tissue specific aspects of genetic modification are withdrawn in view of Applicant's arguments, notably that the Willmitzer reference is not directed to overexpression, but is directed to downregulation of a branching enzyme and that the heterogenous genome of the Desiree variety would likely preclude multiple enzyme isoforms.

Applicant asserts that the Examiner has overlooked that the specification provides guidance for techniques well known in the art that would enable one of skill in the art to determine whether a foreign nucleic acid sequence actually encoded an ADP/ATP translocator. The techniques include, presumably, making and screening cDNA libraries and testing for ADP/ATP translocator activity in recombinant expression systems or locating sequences having the putative translocator activity in public databases using methods of structure function predictions. (response page 4). The specification and not one of skill in the art should provide guidance for practicing the claimed invention. See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a "mere germ of an idea does not constitute [an] enabling disclosure", and that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Applicant asserts that the inventors have demonstrated by experimental evidence that an increase in ADP/ATP translocator activity will lead to an increase in yield (response page 4). This assertion is unfounded for its full scope. The specification is silent on overexpression of foreign nucleic acid molecules encoding a plastidial ADP/ATP translocator in any plant that result in increases in oil content. Applicant is invited to submit a 132 declaration that provides

data to support increases in starch and oil as well as increases in amylose content in plants transformed with a foreign nucleic acid encoding a plastidial ADP/ATP translocator that also includes data with respect to these variables in untransformed control plants.

All claims are rejected.

The claims are deemed free of the prior art given the failure of the prior art to teach plants or plant cells transformed with a foreign nucleic acid sequence encoding a plastidial ADP/ATP translocator having increased oil, starch and amylose content.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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March 9, 2004

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